Remarks

Claims 422-465 are presently pending in the subject application. Claims 441-463 were previously withdrawn from consideration, and claims 422-425, 429, 441-444, 448 and 461 have been amended herein. Claims 464 and 465 and newly added herein.

Reconsideration and allowance are respectfully requested in view of the above amendments and the following remarks.

Claim 422 has been amended herein to specify that the hybrid formed between the first and second base regions of the oligonucleotide contains at least one ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety. Applicants submit that this is a non-limiting amendment since claim 422, as originally presented, provided that the modified form of the oligonucleotide formed a more stable hybrid between the first and second base regions than a hybrid formed between unmodified forms of the first and second base regions under nucleic acid assay conditions. This functional limitation would have indicated to those skilled in the art that the hybrid formed between the first and second base regions of the claimed oligonucleotide included at least one ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety. The amendment to claim 422 is supported by the specification *passim* and, in particular, at page 24, lines 19-22, where it is stated that an oligonucleotide containing one of the disclosed 2'-modifications confers a higher melting temperature to the hybrid than a deoxynucleotide of the same sequence.

Claims 423-425 depend directly from claim 422 and have been amended herein to specify that the claimed 2'-O-alkyl modifications are present in that portion of the first base region capable of forming a hybrid with the second base region under nucleic acid assay conditions. This, of course, is not to suggest that the first base region may not also contain 2'-O-alkyl modifications to nucleotides which are not contained within that portion of the first base region that is capable of forming a hybrid with the second base region under nucleic acid assay conditions.

Claim 429 has been amended herein to indicate that the claimed oligonucleotide is between 10 and 100 bases in length. This amendment is supported by the specification at, for example, page 19, lines 23-25.

Withdrawn claim 441 has been amended herein to depend from amended claim 422, and withdrawn claims 442-444 and 448 have been amended herein to reflect the amendments made to claims 423-445 and 429, respectively. Applicants submit that the amendment to claim 441 herein is not a further limiting amendment, as the "oligonucleotide" language of originally presented claim 441 tracked the language of originally presented claim 422, and the amendment to claim 422 herein is not further limiting for the reasons stated above. Since method claim 441 depends directly from claim 422, Applicants respectfully request rejoinder of claims 441-463 should the Examiner determine that claims 422-440 are allowable. *See* MPEP § 821.04 at 800-63 (August 2001, 8th ed.).

Withdrawn claim 461 has been amended herein to specify that the presence or absence of at least one microorganism or virus in the sample is detected in step c) of the method of claim 441. This amendment is supported by the specification at, for example, page 3, lines 6-14, and the paragraph bridging pages 17 and 18.

Claims 464 and 465 depend from claims 432 and 451, respectively, and recite that a target sequence contained within the nucleic acid analyte includes a double-stranded region. The language of these new claims is supported by the specification at, for example, page 8, lines 11-14, where it is disclosed that the oligonucleotides of the present invention are able to efficiently strand invade double-stranded regions of structured RNA molecules.

Interview Summary

Applicants wish to thank the Examiner for the courtesies extended during an in-person interview with Applicants' representative and one of the inventors of the subject application on August 5, 2003. Applicants note that the Examiner's Interview Summary accurately reflects the matters discussed during the interview, especially the novelty of the claimed invention.

Claim Objections

Claim 422 stands objected to by the Examiner for not including the preposition "of" between "presence" and "a nucleic acid analyte" in line 1 of this claim. Claim 422 has been

amended herein to correct this typographical error, which Applicants thank the Examiner for bringing to their attention. Accordingly, withdrawal of this objection is respectfully requested.

Rejections Under 35 U.S.C. § 102

Claims 422, 423, 425, 426, 429, 434-437 and 440 stand rejected by the Examiner under 35 U.S.C. § 102(b) as being anticipated by Azhayeva *et al.* (*Nucleic Acids Research*, 23(21):4255-4261 (1995)). Applicants respectfully traverse this rejection for the reasons that follow.

Azhayeva is cited by the Examiner for disclosing oligonucleotides having loop structures modified to include 2'-O-methylribonucleotides, where the modified oligonucleotides are more stable than unmodified forms of the oligonucleotides. More particularly, Azhayeva discloses a molecule having first and second base regions modified to include 2'-O-methylribonucleotides, where the first and second base regions have the same base sequence and both hybridize to the same target nucleic acid sequence to form a triplex structure. *See, e.g.*, Figure 1 of Azhayeva. What Applicants claim, however, is an oligonucleotide comprising first and second base regions capable of hybridizing to each other under nucleic acid assay conditions, where the hybrid formed between the first and second base regions includes at least one ribonucleotide modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety. Thus, Azhayeva does not disclose each limitation of the claimed oligonucleotide and, therefore, cannot be relied upon as an anticipatory reference. Accordingly, withdrawal of this rejection is respectfully requested.

Claims 422, 424, 426, 429 and 440 stand rejected by the Examiner under 35 U.S.C. § 102(b) as being anticipated by Lubini *et al.* (*Current Biology*, 1(1):39-45 (1994)). Applicants respectfully traverse this rejection for the reasons that follow.

Lubini is cited by the Examiner for disclosing a self-complementary 2'-O-methylated RNA-DNA chimera that is more stable than the unmodified sequence. In response, Applicants first

observe that while Lubini discloses a ten base sequence containing self-complementary regions, he does not demonstrate or suggest that the disclosed RNA-DNA chimera would in fact be capable of self-hybridization under nucleic acid assay conditions. Moreover, the self-complementary regions of Lubini's RNA-DNA chimera do not include any ribonucleotides modified to include a 2'-O-alkyl substitution to the ribofuranosyl moiety, as required by the claimed invention. Thus, Lubini does not disclose each limitation of the claimed oligonucleotides and, therefore, cannot be relied upon as an anticipatory reference. Accordingly, withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. § 103

Claims 422, 423, 427, 428, 430, 431, 438 and 439 stand rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Azhayeva *et al.* (*Nucleic Acids Research*, 23(21):4255-4261 (1995)) or Lubini *et al.* (*Current Biology*, 1(1):39-45 (1994)) in view of Réfrégiers *et al.* (*Journal of Biomolecular Structure & Dynamics*, 14(3):365-371 (1996)). Since Réfrégiers has a publication date of December 1996, Applicants submit that Réfrégiers is not prior art to the claimed invention, which has a priority date of July 16, 1996. And even if Réfrégiers could be relied upon as prior art to the claimed invention, Applicants further submit that Réfrégiers fails to overcome the deficiencies noted above in the teachings of Azhayeva and Lubini. Accordingly, withdrawal of this rejection is respectfully requested.

Claims 422, 432 and 433 stand rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Azhayeva *et al.* (*Nucleic Acids Research*, 23(21):4255-4261 (1995)) or Lubini *et al.* (*Current Biology*, 1(1):39-45 (1994)) in view of Barry *et al.* (U.S. Patent No. 5,574,145) and Roseau *et al.* (U.S. Patent No. 5,536,638). Applicants submit that Barry and Roseau, both individually and collectively, fail to overcome the deficiencies noted above in the teachings of Azhayeva and Lubini. Accordingly, withdrawal of this rejection is respectfully requested.

REPLY

Serial No. 09/808,558
Atty. Docket No. GP068-05.CN3

Applicants submit that the subject application is in condition for allowance and early Notice to that effect is respectfully requested.

Please charge any fees due in connection with this Reply, including the excess claims fee, to Deposit Account No. 07-0835 in the name of Gen-Probe Incorporated.

Certificate of Transmission

I hereby certify that this correspondence (and any referred to as attached) is being sent by facsimile to 703-746-5206 on the date indicated below to Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Respectfully submitted,

Date: August 12, 2003

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